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The Effects of a Paleolithic Diet on the Risk Factors of Chronic Disease

Abstract

Background: The modern western diet has been one of the major suspects in the rise of chronic disease such as diabetes, cardiovascular disease, and obesity. The Paleolithic diet may be a more metabolic fit for humans compared to current contemporary diets. The purpose of this review is to investigate the effects of a Paleolithic diet on the risk factors of patients with chronic disease in isolation and compared to contemporary diets.

Methods: An exhaustive search of online medical literature was performed using Medline-OVID, Web of Science, and CINAHL-EBSCO. Keywords used included: Paleolithic diet, palaeolithic diet, paleo diet, and hunter gatherer diet. Eligible studies were assessed using the GRADE criteria.

Results: Four articles met eligibility criteria. Two of the articles were by the same author discussing the same study but with different data that are relevant to this review. Two of studies were randomized control trials while one was specifically a randomized crossover trial. There are some consistent results regarding significant improvement of weight, waist circumference, and triglycerides in the Paleolithic diet groups when compared to the contemporary diet groups. The overall quality of the original studies are low to moderate due to some limitations. Further studies can minimize these limitations to improve quality of evidence in regards to the effects of a Paleolithic diet on patients with chronic disease.

Conclusion: Thus far, studies investigating a Paleolithic diet do not provide enough evidence to support its place as a universally recommended diet, but the diet can be an option for medical providers to discuss with patients to combat chronic disease.

Keywords: Paleolithic diet, palaeolithic diet, chronic disease, diabetes, obesity, cardiovascular disease, risk factors

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The Effects of a Paleolithic Diet on the Risk Factors of Chronic Disease

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ABSTRACT

Background: The modern western diet has been one of the major suspects in the rise of chronic disease such as diabetes, cardiovascular disease, and obesity. The Paleolithic diet may be a more metabolic fit for humans compared to current contemporary diets. The purpose of this review is to investigate the effects of a Paleolithic diet on the risk factors of patients with chronic disease in isolation and compared to contemporary diets.

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Results: Four articles met eligibility criteria. Two of the articles were by the same author discussing the same study but with different data that are relevant to this review. Two of studies were randomized control trials while one was specifically a randomized crossover trial. There are some consistent results regarding significant improvement of weight, waist circumference, and triglycerides in the Paleolithic diet groups when compared to the contemporary diet groups. The overall quality of the original studies are low to moderate due to some limitations. Further studies can minimize these limitations to improve quality of evidence in regards to the effects of a Paleolithic diet on patients with chronic disease.

Conclusion: Thus far, studies investigating a Paleolithic diet do not provide enough evidence to support its place as a universally recommended diet, but the diet can be an option for medical providers to discuss with patients to combat chronic disease.

Keywords: Paleolithic diet, palaeolithic diet, chronic disease, diabetes, obesity, cardiovascular disease, risk factors

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LIST OF ABBREVIATIONS

AUC	Area Under the Curve
BMI	Body Mass Index
DBP	Diastolic Blood Pressure
HbA1C	Glycated Hemoglobin, Hemoglobin A1C
HDL	High-Density Lipoprotein
LDL	Low-Density Lipoprotein
MAP	Mean Arterial Pressure
NNR	Nordic Nutrition Recommendation (diet)
OGTT	Oral Glucose Tolerance Test
PD	Paleolithic Diet
SBP	Systolic Blood Pressure
TG	Triglycerides

The effects of a Paleolithic diet on the risk factors of chronic disease

BACKGROUND

Chronic diseases such as diabetes, obesity, and cardiovascular disease have been shown to be major causes of comorbidities and mortalities in the Western world.¹ For example, diabetes was the seventh leading cause of death in the United States in 2010, and it may even possibly be underreported as a cause of death. Diabetes has many complications if left untreated, including lack of blood sugar control, hypertension, dyslipidemia, rising risk of heart attack and stroke, diabetic retinopathy, and kidney disease.² In addition to lack of exercise and exposure to environmental chemicals such as cigarette smoke, poor nutrition has been a main cause in the rise of chronic disease.

The human diet has changed drastically ever since the agricultural revolution (Neolithic era) after the Paleolithic era.³ Humans have not evolved at the same pace to adequately metabolize the food that is in excess in the modern world and was scarce in the Paleolithic era. For example, while the vast majority of the Paleolithic diet (PD) of hunter-gatherers involved lean meat, fish, fruits, vegetables, and nuts, an average 64.7% of the American diet is made up of sugars, fats and oils, and grain products.^{4,5}

There have been short-term studies of healthy human subjects that have shown improvement with some chronic disease risk factors after being on a PD.^{6,7} In Osterdahl et al,⁶ observation of 14 healthy volunteers on the PD for 3 weeks showed significant decreases in weight, waist circumference, and systolic blood pressure (SBP) from baseline. In Frassetto et al,⁷ nine non-obese sedentary healthy volunteers were on the PD for 10 days which resulted in significant decreases in their diastolic blood pressure (DBP) and mean arterial pressure (MAP) from baseline.

In addition to increased physical exercise and abstinence from harmful environmental chemicals, many diets have been offered as a solution to combating chronic disease, whether they are clinically recommended or not. Osterdahl et al⁶ and Frassetto et al⁷ has provided some evidence in

support of the PD improving several chronic disease risk factors in healthy participants. The aim of this review is to find out if the Paleolithic diet can significantly reduce risk factors of patients with chronic disease in isolation and when compared to contemporary diets.

METHODS

An exhaustive online search of medical literature was performed using MedLine-OVID, Web of Science, and CINAHL-EBSCO databases. The keywords used during this search were: paleolithic diet, paleo diet, palaeolithic diet, and hunter gatherer diet. Eligibility criteria were: English language articles, randomized trials, studies using human subjects, inclusion criteria participants with chronic disease, measures of cardiovascular disease, diabetes, and obesity were used as outcome variables, and the Paleolithic diet was compared contemporary diets. An altered version of the Paleolithic diet was not considered a contemporary diet. Applicable articles were assessed for quality using the Grading of Recommendations, Assessment, Development, and Evaluation (GRADE).⁸

RESULTS

An initial search of Medline-OVID using the aforementioned keywords revealed 45 articles. Three articles^{9,10,11} met eligibility criteria. It is important to note that two^{9,10} of these three articles are based on the same study with data completed from the same patient population. The main difference from the original study by Lindeberg et al⁹ and the second article¹⁰ published in 2010 by mostly the same authors was the separate sets of data that were discussed. Both articles were included in this review since they contain different outcome variables that are relevant for this systematic review. An initial search of Web of Science with the keywords resulted in 421 articles of which six were randomized trials. One of these articles¹² met eligibility criteria and did not appear in the Medline-OVID search. A search of CINAHL-EBSCO with the keywords revealed 39 articles of which none met eligibility criteria and was exclusive to CINAHL compared to the aforementioned database searches. In total, four articles were assessed for this systematic review (See Table I).

Lindeberg et al (2007)

This 12 week randomized control trial⁹ was designed to compare patients with ischemic heart disease (IHD) with either type 2 diabetes or glucose intolerance and a waist circumference of >94 cm randomized to the PD or Mediterranean-like (Consensus) diet. Primary outcome variables focused on glucose intolerance. All participants were patients recruited from the Coronary Care Unit at Lund University Hospital in Sweden. Inclusion criteria was ongoing coronary syndrome, a diagnosed history of myocardial infarction, diagnosed coronary stenosis of >30% by angiogram, and percutaneous coronary intervention or coronary artery bypass surgery. Patients were excluded if they had a BMI <20 kg/m², serum creatinine >130 µmol/l, poor general condition, dementia, unwillingness/inability to prepare food at home, participation in another trial, chronic inflammatory bowel disease, type 1 diabetes and treatment with hypoglycemic agents, warfarin or oral steroids. Out of 38 eligible subjects, 29 male patients were included in the study after the other nine were excluded due to worsening general condition (n = 4), unwillingness to continue (n = 3, all from the PD group), or missing oral glucose tolerance test (OGTT) data (one in each group). Eligible participants were informed about the intent to compare two healthy diets but were not told if one was superior to the other in reducing weight or improving glucose tolerance.⁹

Twenty-nine subjects were randomized into a PD group (n = 14) and Consensus group (n = 15). Before the study, the authors calculated that 12 patients would be needed in each group in order to detect, with a 80% power and at a significance level of 5%. The PD was based on lean meat, fish, fruits, leafy and cruciferous vegetables, root vegetables (including restricted amounts of potatoes), eggs and nuts while the Consensus diet was based on whole-grain cereals, low-fat dairy products, potatoes, legumes, vegetables, fruits, fatty fish and refined fats rich in monounsaturated fatty acids and alpha-linolenic acid. Both groups were prognostically balanced except for a difference (p-value = 0.01) of age in years where the PD group was older (65 +/- 10) than the Consensus group (57 +/- 7). Both groups

were given dietary advice, food recipes, and information on the main concepts of their specified diet. Both groups had small differences in education intensity pertaining to their diet and were advised about regular physical activity in an equal fashion. Due to the small difference in dietary education provided to both study groups, the authors did not consider a “usual care” control group necessary. There was no mention of blinding in the article.⁹

Primary endpoints decided on before the start of the study were changes in the area under the curve between 0 and 120 minutes during OGTT for plasma glucose (AUC Glucose₀₋₁₂₀) and plasma insulin (AUC Insulin₀₋₁₂₀), along with changes in body weight and waist circumference. Diet surveillance was done with a single 4 consecutive day weighted food record that included a weekend day. This was done 15 +/- 5 days after the initiation of diet change. Patients were given a digital weighing scale, with a zeroing function, to weigh their food. The authors checked for under-reporting by comparing food records with baseline weight and achieved weight loss, and by evaluating distribution and amount of consumed food.⁹

Results were analyzed with a confidence interval of 95% and significant p-value of <0.05 (See Table II). There was no significant differences between study groups in weight loss at 6 weeks from baseline or 12 weeks from baseline although both had significant weight loss within their groups at the aforementioned checkpoints. Decrease of waist circumference was significant within both groups at 6 and 12 weeks from baseline while the PD group had a significant decrease compared to the Consensus group at the same checkpoints. AUC Glucose₀₋₁₂₀ and AUC Insulin₀₋₁₂₀ were both significantly decreased within the PD group at 6 weeks and 12 weeks from baseline. The same measures were not significant within the Consensus group except for a significant decrease of AUC Insulin₀₋₁₂₀ at 6 weeks from baseline. The PD group had a significant decrease of AUC Glucose₀₋₁₂₀ compared to the Consensus diet at 12 weeks from baseline while there was no significant difference of AUC Insulin₀₋₁₂₀ between groups at the same checkpoint. Decrease in fasting plasma glucose was significant within the PD diet at 12 weeks

from baseline while the same measure was insignificant in the Consensus diet but there was no significant difference between the groups. There was no significant decrease of HbA1C within or between study groups at 6 or 12 weeks from baseline.⁹

Limitations of this study include a dropout of nine eligible participants though they were not part of the intention to treat patients and the method of randomization was not noted in the article. Although there was a check for underreporting of diet adherence, only one 4 consecutive day diet report was used with each participant for the duration of the 12 weeks.⁹

Jönsson et al (2010)

This article is a review of the trial done by Lindeberg et al⁹ in which the majority of the same authors of the original study discuss results that were not included in the first published article. These results of the second article pertain to data of subjective ratings of satiety at meals, fasting plasma leptin, plasma leptin receptor, and free leptin index drawn from the same PD and Consensus groups. Satiety data was based on a Satiety Quotient. The Satiety Quotient is calculated by the difference of satiety ratings pre-eating episode and post-eating episode divided by food intake of the eating episode.¹³ The relevance of including the hormone, leptin in the study is due to its effects on appetite, blood pressure, and energy homeostasis among other applications.¹⁴ Leptin binds to soluble leptin receptors (SLR) which play a major role in activation of leptin.^{15,16} Free leptin index ("ratio of levels of circulating leptin and SLR") has been shown to have a positive correlation with risk factors such as body fat mass and hypertension.^{17,18} Refer to above⁹ in regards to overall study methods and limitations of the original study.

There was no significant difference in change of satiety after meals between the PD and Consensus groups but the PD group had a significantly lower mean average of energy from food and drink per meal as well as per day compared to the Consensus group. Increase in fasting plasma leptin

was significantly higher within both groups at 6 and 12 weeks from baseline. Relative change in fasting plasma leptin was only significantly higher in the PD group compared to the Consensus group at 6 and 12 weeks from baseline when one outlier was excluded. There was no significant difference in the relative change of fasting plasma leptin receptors between groups at 6 or 12 weeks from baseline. There was no significant difference in relative changes of free leptin index between both groups at 6 or 12 weeks from baseline. Relative changes in leptin and changes in weight and waist circumference correlated significantly in the PD group but not in the Consensus group. The data of improved glucose tolerance in the original study did not correlate with the new data regarding satiety, leptin, or leptin receptors.¹⁰

Jönsson et al (2009)

This was a separate study done by mostly the same authors of Lindeberg et al in 2007. It was a randomized cross-over comparison of type 2 diabetes patients (not being treated with insulin) assigned to either the PD or Diabetes diet (based on current recommendations¹⁹) groups initially with cardiovascular risk factors as the outcomes variables. The study length was 6 months with patients switching their initially assigned of diets after the end of 3 months to the other diet. There was no washout period before the crossover. Participants were recruited from three primary health care units in the Lund area in Sweden. Inclusion criteria was type 2 diabetes, C-peptide value above zero, unaltered medical diabetes treatment and stable weight for since three months before start of study, HbA1C above 5.5%, creatinine below $\mu\text{mol/L}$, liver enzymes below their respective upper reference values, no chronic oral or injection steroid treatment and no acute coronary event or change in beta blockers or thyroxin since six months before start of study. Patients were excluded during the process of the study if they had changes or addition to the aforementioned medications, creatinine and liver enzymes increasing above the aforementioned values, receiving warfarin treatment, an acute coronary event, physical or psychological illness, or circumstances preventing them from completing the study.

Exceptions to the exclusion in regards to medication changes during the study were made to pertaining patients if their removal would have not changed the outcome data.¹¹

Out of 17 eligible patients, 13 (10 men and 3 women) were included in the study. The other four patients were excluded due to either: being included incorrectly because of ongoing warfarin treatment, unwilling to continue due to GI symptoms, development of leukemia, or development of heart failure. Prior to the study, it was calculated that a total of 15 patients would be required to detect, with a 80% power and at significance level of 5%. As with Lindeberg et al⁹, participants were not given any information regarding a superior diet and the goal of patient education in both diets was to be equal as much as possible to prevent bias. Seven patients were randomized to the PD while six were randomized to the Diabetes diet. Randomization was done using identical envelopes for both diets. No blinding was done on participants or investigators of the study after randomization. No control group was included in the study as each participant were their own control as they had an equal trial length of both diets (3 months). Both groups were prognostically balanced except the group starting with the PD had a lower baseline HbA1C (p-value = 0.06), significantly lower baseline fasting plasma glucose (p-value = 0.02), and significantly lower baseline AUC glucose₀₋₁₂₀ (p-value = 0.046). As mentioned above, no washout period was performed in this study but mean values of outcome variables and reported dietary intakes for the group starting with Paleolithic diet was compared with the group starting with Diabetes diet in order to check for carry-over effects. As with Lindeberg et al⁹, a four consecutive day weighed food record was done by each patient in the same manner except that one was done 6 weeks after starting each diet.¹¹

Outcome variables for this study included HbA1C, cholesterol, LDL levels, HDL levels, triglycerides (TG), systolic blood pressure (SBP), diastolic blood pressure (DBP), weight, body mass index (BMI), waist circumference, fasting plasma glucose, fasting plasma insulin, AUC Glucose₀₋₁₂₀, and AUC Insulin₀₋₁₂₀. At the end of the three months from baseline, the group that started with the PD had a more significant relative decrease HbA1C, TG, DBP, weight, BMI, and waist circumference with a more

significant relative increase in HDL when compared to the group that started with the Diabetes diet. There was no significant difference between groups in regards to relative change of cholesterol, LDL, SBP, fasting plasma glucose, fasting plasma insulin, AUC Glucose₀₋₁₂₀, and AUC Insulin₀₋₁₂₀ at the end of three months from baseline. At the end of six months, there were no significant differences in cholesterol, LDL, HDL, TG, Weight, BMI, waist circumference, SBP, DBP, fasting plasma glucose, or fasting plasma insulin between the two groups. Possible carryover effects were noted with the measurement of HbA1C at six months from baseline as the group starting with the PD had a significantly lower value than the comparison group. No carry-over effects were found in reported dietary intake although this particular data was not shown in the article.¹¹

Limitations of this study include lack of blinding after randomization and a small patient population that was lower than the pre-study power calculation. Similarly to Lindeberg et al,⁹ only a single four consecutive day diet report was used with each participant for each three month period.

Mellberg et al (2014)

This was a randomized control trial¹² that compared 70 obese postmenopausal women on either a PD or Nordic Nutrition Recommendations (NNR) diet²⁰ for two years. The primary outcome was change in fat mass. Recruitment was done through advertisements of local newspapers of which 210 women were interested in study participation. Additional inclusion criteria were no smoking and a BMI of equal or greater than 27 kg/m². Subjects were excluded if they were on a restricted or vegetarian diet, had allergies to important foods of the study diets, had a history of heart disease, kidney disease, thyroid disease, osteoporosis, diabetes, abnormal fasting plasma glucose levels, high blood pressure, on hormone replacement therapy, taking beta-blockers, statins, or any medication for mental health disorders.¹²

The study authors estimated a significant outcome ($p < 0.05$) with 80% power would require at least 35 subjects in each diet group. Block randomization was done by a statistician blinded to the study. All study personnel (except the dietitians) were blinded to the dietary allocation of the participants. One trained dietitian per diet held 12 educational group sessions with their respective diet group throughout the 2 year period. Data was assessed with an intention-to-treat analysis. Both groups were prognostically balanced except for higher HDL in the PD group ($p = 0.01$).¹²

There was a significant decrease of fat mass, body weight, waist circumference, and sagittal abdominal diameter in the PD group compared to the NNR group at 6 months from baseline. There was no significant difference between groups with the same anthropometric measures at 24 months from baseline. The PD group showed a significant decrease in TG at 6 and 24 months from baseline when compared to the NNR group. This was not true for other outcome variables in the study, including fasting insulin, glucose, SBP, DBP, cholesterol, HDL, and LDL.¹²

Limitations of the study includes the high dropout rate in both groups at 6 month ($n_{PD} = 1$ and $n_{NNR} = 8$) and 12 month follow-up ($n_{PD} = 7$ and $n_{NNR} = 5$) which resulted in a study population that was lower than the required 35 subjects in each diet estimated to have a $p < 0.05$ at 80% power. In addition, there was no third (control) group to compare to both the PD and NNR groups.¹²

DISCUSSION

The modern western diet has been one of several major societal factors attributed to the increase in chronic disease in modern civilization. More specifically, the increase of surplus in foods that were scarce before the industrialized world and especially before the agricultural revolution, has been faster than what the human body can adjust to metabolize adequately.³ There have been some evidence to show that a diet more closely resembling that of what a hunter-gatherer consumed in the period before the agricultural revolution, the Paleolithic era can help decrease risk factors of chronic

disease.^{6,7} These benefits are generally held consistent with the studies⁹⁻¹² of this systematic review.

Although the overall quality of these studies is low to moderate, the possibly strong advantages of the Paleolithic diet outweigh its low risk of harm. Thus, clinicians should consider possibly recommending the PD to patients with chronic diseases such as diabetes, obesity, and cardiovascular disease.

In the three reviewed original studies, decrease in weight and/or waist circumference was significant within the PD groups across the studies.^{9,11,12} The same measures were significant between study groups of Jönsson et al (2009)¹¹ at three months from baseline and Mellberg et al¹² at six months from baseline. The authors of Mellberg et al¹² proposed that lack of significance in these measures between intervention diets at 24 months may be due to patients of the PD group having decreased adherence to their diet in the long term. This may be due to lack of motivation and financial burden of the Paleolithic diet's main foods (such as lean meats, fruits, and vegetables).¹² Lack of significance between dietary interventions in Lindeberg et al⁹ for weight loss and waist circumference may indicate that a Mediterranean (Consensus) diet has more similar strength of effect on such outcomes to a PD than a Diabetic or NNR diet.

Fasting plasma glucose and fasting plasma insulin decreased within the PD groups of all three studies^{9,11,12} with only Mellberg et al¹² showing no significance in either measure, though this may be due to the pertaining subjects having a normal glucose tolerance at baseline. This is supported as both PD and NNR groups were prognostically balanced overall. Furthermore, the NNR group also showed no significant decrease of fasting plasma glucose and fasting plasma insulin within the diet group.¹² There was no significant relative decrease of plasma glucose between the PD and the other contemporary diets in all three studies.^{9,11,12}

The findings discussed in Jönsson et al (2010)¹⁰ showed a similar mean satiety ratings between dietary groups with the PD group consuming less energy from food and drink. The importance of this

finding is that PD foods can be more satiating than recent dietary recommendations for diabetes patients. This can possibly have implications on helping diabetic patients improving their glucose intolerance through weight loss from eating less calories with more satiating foods in the PD.¹⁰

A full lipid panel of outcomes (cholesterol, HDL, LDL, and TG) was measured in only Jönsson et al (2009)¹¹ and Mellberg et al.¹² Of these outcomes, only TG showed consistent results between the two studies in regards to a relative significant improvement between the PD group and contemporary diet groups. This may be due to the difference of the contemporary diets (in this case, Diabetic diet and NNR diet). Nonetheless, there is an improvement in cholesterol, HDL, LDL, and TG within the PD group in both studies, though not each outcome was significant.^{11,12}

The main limitations of the studies included in this systematic review are lack of double-blinding, lack of true control groups to the intervention diets, small study population size, and attrition bias.⁹⁻¹² Specifically in Jönsson et al (2009),¹¹ the lack of a washout period possibly resulted in carryover effects of HbA1C in this randomized cross-over trial although there was no carryover effects for the dietary intake change (See Table I). This shows the participants adhering to the diets but it was only based on a single four consecutive day diet intake report. In addition, a washout period would have given a more clear effect of the PD on HbA1C levels in both groups as this variable is essentially a biomarker of blood sugar levels within the past 2 to 3 months. Generally, double-blinding in dietary studies are difficult to perform as subjects can easily distinguish between the key components of diets, especially with the guidance of study dietitians. Further studies can minimize this by blinding investigators who are involved with data collection. Control groups can be hard to implement as there is no “universal consensus diet” as well as a lack of utility in comparing healthy patients and those with chronic disease. The authors of the reviewed studies tried to minimize the lack of blinding and control groups by equalizing the patient education between diet interventions as much as possible.⁹⁻¹² An

alternative to using a vague “control diet group” is to have several contemporary diets (more than one) to compare to the PD in one single study.

CONCLUSION

There is some evidence presented in observational studies of healthy patients and RCTs of patients with chronic disease that a Paleolithic diet can improve various risk factors of diabetes, cardiovascular disease, and obesity. Furthermore, the Paleolithic diet has shown to be as effective or more effective in improving many of these risk factors in comparison studies with contemporary diets. This current collective evidence is not strong enough to change dietary guidelines for patients with chronic disease due to several limitations in the reviewed studies. Future studies should have outcome measurements for both short term (<3 months) and long-term (>1 year) checkpoints, at least two common contemporary diets to compare to the PD, maximized blinding per a diet comparison model, and regular intervals of patients recording their food intake. There are other measured outcomes (such as high protein and low calcium intake from the PD) in the evaluated studies that were consistently significant but not discussed in this systematic review. These outcomes should be further researched to find out if such dietary intake will adverse effects that outweigh the possible significant benefits of the Paleolithic diet. However, the PD currently has enough evidence to be an option for medical providers to discuss with their diabetic, obese, or cardiovascular disease patients without contraindications. In addition to exercise and avoidance of environmental toxins, the PD option may be able to significantly improve the health and quality of life in these chronic disease patients compared to other diet alternatives.

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TABLES

Table I. GRADE Assessment: Characteristics of Reviewed Studies							
Design	Included Outcomes	Downgrade Criteria					Quality
		Limitations	Indirectness	Imprecision	Inconsistency	Publication bias likely	
Lindeberg et al (2007) ⁹ and Jönsson et al (2010) ¹⁰							
RCT	Weight, Waist circumference, Fasting plasma glucose, HgbA1C, Cholesterol, Satiety	Serious limitations ^a	No serious indirectness	No serious imprecision	No serious imprecision	No bias likely	Moderate
Jönsson et al (2009) ¹¹							
Randomized Crossover Trial	Weight, Waist circumference, Fasting plasma glucose, HgbA1C, Cholesterol, HDL, LDL, TG, SBP, DBP	Very serious limitations ^{a,b}	No serious indirectness	Serious imprecision ^c	No serious imprecision	No bias likely	Very low
Mellberg et al (2014) ¹²							
RCT	Weight, Waist circumference, Fasting plasma glucose, Cholesterol, HDL, LDL, TG, SBP, DBP	Very serious limitations ^{a,d}	No serious indirectness	No serious imprecision	No serious imprecision	No bias likely	Low
^a Lack of mention of blinding of the researchers who were collecting the data							
^b Failure to fully account for carry-over effect and lacked a wash-out period							
^c Small sample size							
^d Large percentage of attrition in both study groups							

Table II. Summary of Findings

	Number of Patients				Outcomes: Comparing changes in outcomes between diets (Significant p-values <0.05)											
Study	Treatment Group = Paleolithic Diet (PD)	Comparison Diet (CD)	Patient Population	Study Length	Weight	Waist Circumference	Fasting Plasma Glucose	HgbA1C	Cholesterol	HDL	LDL	Triglycerides	SBP	DBP	Satiety	
Lindeberg et al (2007) ⁹ and Jönsson et al (2010) ¹⁰	n = 14	(Mediterranean-like Diet, AKA Consensus Diet) n = 15	Men with ischemic heart disease, waist circumference >94 cm, and known diabetes or increased blood glucose	12 weeks	Change 0-12 weeks											
					kg	cm	mmol/l	%	mg	N/A ^e	N/A	N/A	No decrease in blood pressure within study groups. ^f	RS/MJ ^g		
					PD = -5.0 +/- 3.3	PD = -5.6 +/- 2.8	PD = -1.7 +/- 1.7	PD = -0.13 +/- 0.26	PD = 397 +/- 192					PD = 2.5 +/- 1.3		
					CD = -3.8 +/- 2.4	CD = -2.9 +/- 3.1	CD = -0.9 +/- 1.8	CD = -0.03 +/- 0.39	CD = 295 +/- 122					CD = 1.6 +/- 0.5		
					p = 0.3	p = 0.03	p = 0.2	p = 0.4	p = 0.11					p = 0.03		
Jönsson et al (2009) ¹¹	(Paleolithic Diet first 3 months) n = 7	(Diabetes Diet first 3 months) n = 6	Men and women with Type 2 DM without insulin treatment	6 months (Crossover study)	Change from 0-3 months (Change at end of 1 st diet from baseline) ^h											
					kg	cm	mmol/l	%	mmol/l	mmol/l	mmol/l	mmol/l	mmHg	mmHg	N/A	
					BL = 87 +/- 17	BL = 103 +/- 14	BL = 7.8 +/- 1.2	BL = 6.6 +/- 0.6	BL = 4.4 +/- 1.1	BL = 1.28 +/- 0.22	BL = 2.9 +/- 0.9	BL = 1.5 +/- 0.7	BL = 150 +/- 21	BL = 83 +/- 10		
					PD = 81 +/- 13	PD = 94 +/- 9	PD = 7.0 +/- 1.4	PD = 5.5 +/- 0.7	PD = 4.3 +/- 1.2	PD = 1.34 +/- 0.30	PD = 2.7 +/- 1.0	PD = 1.0 +/- 0.5	PD = 140 +/- 12	PD = 79 +/- 6		
					CD = 84 +/- 15	CD = 98 +/- 11	CD = 7.5 +/- 1.4	CD = 5.9 +/- 0.9	CD = 4.5 +/- 1.2	CD = 1.26 +/- 0.23	CD = 2.8 +/- 1.1	CD = 1.5 +/- 0.7	CD = 149 +/- 22	CD = 83 +/- 9		
					p = 0.01	p = 0.02	p = 0.08	p = 0.02	p = 0.3	p = 0.03	p = 0.5	p = 0.003	p = 0.13	p = 0.03		
Mellberg et al (2014) ¹²	n = 35	NNR Diet n = 35	Obese, postmenopausal, non-smoking women	24 months	kg	cm	mmol/l	N/A	mmol/l	mmol/l	mmol/l	mmol/l	mmHg	mmHg	N/A	
					P value between study groups regarding change in outcome variables at 6 months from baseline											
					p = <0.001	p = <0.01	p = NS ⁱ	N/A	p = NS	p = NS	p = NS	p = NS	p = <0.001	p = NS		p = NS
					P value between study groups regarding change in outcome variables at 24 months from baseline											
p = NS	p = NS	p = NS	N/A	p = NS	p = NS	p = NS	p = NS	p = 0.004	p = NS	p = NS						

^e Need not apply as study does not include the pertaining data.^f Author states “that there was no decrease blood pressure” in study patients. No data was shown in article pertaining to decrease in blood pressure within or between study groups.^g Quotient of mean change in satiety during meal (RS) and mean energy from food and drink per meal (MJ).^h Data involving outcome variables after patients switched diets at 3 months from baseline was not included in this summary table. The focus of this summary is to compare effects of the diets on the outcome variables without having to take into account for crossover effects that would be applicable 3 to 6 months from study baseline.ⁱ P-value is not significant.